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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,581	01/17/2006	Thomas Link	23062	7537

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EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,581	LINK ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/05, 4/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-27 are currently pending in this application.

Election/Restrictions

Applicant's election with traverse of the species "CHO cells" and "immunoglobulins" in the reply filed on 5/13/08 is acknowledged. The traversal is on the ground(s) that the species in claims 21 and 23 are unified by a special technical feature, i.e. the method of claim 16. This is not found persuasive because applicant has not applied the correct standard for evaluating inventive unity among chemical species. As discussed at length on pages 3-4 of the restriction requirement mailed 4/14/08, alternatives of chemical compounds (such as the proteins in claim 23) are not art-recognized equivalents for each other because they do not share a significant structural element. The proteins in claim 23 have diverse amino acid structures and diverse functions in cells and organisms and cannot be considered to be equivalents for each other in any manner. Similarly, the cells in claim 21 are isolated from distinct tissues and have distinct properties. Applicant has made no argument that this is not the case.

The requirement is still deemed proper and is therefore made FINAL. Examination will commence at this time on claims 16-27 to the extent they read on the elected species where applicable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing two specific polypeptides from two specific cell types by culturing said cells in a particular nutrient media, does not reasonably provide enablement for a method for making any given substance, including identifying the cells and media conditions that would yield its production. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The claims are drawn to a method for producing a substance (i.e., any substance) by culturing cells that produce said substance in a media that "results in a [particular] degree of glucose limitation (DGL)." In some dependent claims, the DGL is pointed out. In some dependent claims, the amount of glucose in the media is described in terms of its consumption by cells. In some dependent claims, the type of cell or type of substance is pointed out. Some dependent claims further describe the conditions of

the culturing step. As discussed below in the rejections under 35 U.S.C. § 112, second paragraph, the claims are so indefinite that they preclude meaningful examination.

The instant method requires as a starting product cells that produce the substance of interest. The scope of the substance is not particularly limited in the claim; the term "substance" refers to any and all matter. Identifying cells that produce each and every given substance would require undue experimentation; the specification and art provide no guidance for identifying cells that produce, e.g., high-energy plasma or moon rocks. Even if the term "substance" were interpreted as "naturally occurring bioactive substance," the specification would fail to be enabling because there is guidance for identifying a cell that produces each and every bioactive substance and culturing it in a media that meets the claim's criteria. Many bioactive substances are products of non-mammalian organisms, e.g. taxol (a plant product) and botulinum toxin (a bacterial product). The scope of the specification is limited to methods for the production of a few specific polypeptides from a few mammalian cell types that appear to have been engineered for the specific purpose of producing those polypeptides (specification, page 7, paragraph 2).

Even if the claims were interpreted as being drawn to a method for producing a recombinant polypeptide from a mammalian cell engineered to overexpress that polypeptide, the specification would still fail to be enabling across the claim's entire scope. The method of claim 16 requires culturing the cells in a media that results in a "degree of glucose limitation (DGL)" that is defined in terms of its relationship to the DGL required to maintain the cell in some way and in terms of a ratio of "currently

observed" glucose consumption rate to "maximum known" rate. Neither of these variables is properly defined in the specification such that the skilled artisan could identify the components of the media that would yield the desired DGL for a given cell type. The specification provides no guidance for identifying these parameters for a given cell, much less guidance for selecting media components that would yield the desired DGL.

Finally, applicants present a single working embodiment in which two specific proteins (MUC-Ig2a fusion protein and "MUC-C-term," allegedly a truncation mutant of MUC) are produced from CHO cells that appear to have been engineered specifically for the production of these fusion proteins. The specification does not define any of the media used in the methods by listing components and their concentrations therein. At page 7, paragraph 3, the specification refers to "ProCHO4-CDM" media but provides no further description of this media. While a singular, narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the lack of direction applicants present, provides additional weight to the lack of enablement in consideration of the *Wands* factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

Claims 16-27 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co.*, Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See M.P.E.P. § 2163.02. In this case, the skilled artisan would not have reasonably concluded at the time of the invention that applicant was in possession

of the entire invention as claimed because the media required to carry out the claimed method is not described in the specification.

As discussed in the enablement rejection, the claims are drawn to a method of producing a substance by culturing cells that produce that substance in a media that provides a desired DGL. However, the specification provides insufficient description of the media that the skilled artisan would immediately envisage the components necessary to yield a given substance from a given cell.

The issue in this application is similar to that considered in *University of Rochester v. G.D. Searle & Co.,* 68 USPQ2d 1424 (DC WNY 2003). In *Rochester*, at issue was a patent directed to method for inhibiting prostaglandin (PGHS-2) synthesis in a patient using an unspecified compound. The District Court of Western New York evaluated the level of disclosure required to satisfy the written description. In their decision (which was later affirmed by the CAFC), the District Court wrote, "The real issue here is simply whether a written description of a claimed method of treatment is adequate where a compound that is necessary to practice that method is described only in terms of its function, and where the only means provided for finding such a compound is essentially a trial-and-error process."

The patent in *Rochester* does no more than describe the desired function of the compound called for, and it contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. The specification of the patent in *Rochester*

states that the invention comprises, inter alia, "assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product; and methods of treating diseases characterized by aberrant PGHS-2 activity using such compounds." Nowhere, however, does it specify which "peptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting PGHS-2.

The *Rochester* court cited the CAFC in *Enzo Biochem, Inc. v. Gen-Probe Inc.,* 296 F.3d 1316 (63 USPQ2d 1609), which adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics *when coupled with a known or disclosed correlation between function and structure* ... ." *Enzo*, 296 F.3d at 1324-25 (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added)).

The *Rochester* court also cited the CAFC in *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 [43 USPQ2d 1398] (Fed. Cir. 1997), in which the court drew a distinction between genetic material and other chemicals; in drawing this distinction, however, the court also stated that "[i]n claims involving [non-genetic] chemical materials, generic formulae *usually indicate with specificity what the generic claims encompass*. One skilled in the art can distinguish such a formula from others and *can identify many of the species* that the claims encompass. Accordingly,

such a formula is normally an adequate description of the claimed genus." 119 F.3d at 1568 (emphasis added). There is no such specificity here, nor could one skilled in the art identify any particular media encompassed by the claims.

The "written description" requirement may be satisfied by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that **fully set forth** the claimed invention. See *Noelle v. Lederman*, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) and *Lockwood v. American Airlines, Inc.*, 107 F.3d at 1572, 41 USPQ2d at 1966. A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3 at 1568, 43 USPQ2d at 1406 (Fed. Cir. 1997) (discussing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). In *Fiers v. Ravel*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (1993), the CAFC found that "a mere wish or plan for obtaining the claimed chemical invention" is not sufficient to describe a chemical invention (discussed in *Eli Lilly* at 1404).

The fact pattern in this case is similar to that in *Rochester.* In *Rochester*, there were no compounds known to have the required function, and in the instant application, no media suitable for the method are particularly disclosed and described. The key similarity between the cases, and the one relevant to this ground of rejection, is the fact that no method is provided for identifying components having the function necessary to carry out the method, and no component is particularly described. For this reason, the rejection due to lack of written description is proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is incomplete in the absence of a recovery step for the product produced. While there is no specific rule or statutory requirement which specifically addresses the need for a recovery step in a process of preparing a composition, it is clear from the record and would be expected from conventional preparation processes that the product must be isolated or recovered. Thus, the claims fail to particularly point out and distinctly claim the **complete** process since the recovery step is missing from the claims. The metes and bounds of the claimed process are therefore not clearly established or delineated. Clarification is required.

Claim 16 requires culturing cells in "a nutrient media that results in a degree of glucose limitation (DGL)," wherein the DGL is further defined in terms of a ratio and in terms of its relationship to a minimum level. These limitations do not particularly define the media by its structural and physical properties, but rather wholly by its function, which is improper. See *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). The claim does not particularly point out what components are necessarily included and excluded from the media. Clarification is required.

Claim 16 refers to "the DGL needed for maintenance of the cell," but this term is not clear. First, the nature of the "maintenance" is not pointed out; it is not clear whether

the cell must simply survive or whether it must produce the substance of interest. Second, it is not clear how this value would be determined for any given cell. Clarification is required.

Claim 16 requires that the media's composition depend on two variable elements, which renders the claim indefinite. In the media of claim 16, the DGL ratio between the "**currently** observed specific consumption rate" and the "maximum **known** specific consumption rate" must be equal to or below 0.5, but the terms "currently observed" and "maximum known" do not place any particular limits on these rates. There is no basis provided for the comparative term "currently," and the claim indicates by use of the term "maximum known rate" that the scope may change depending on some unknown future findings of skilled artisans. There is no guidance for identifying these numbers for a given cell under given conditions. Clarification is required.

Claim 16 refers to "consumption rate," but it is not clear what is being consumed. Clarification is required.

In short, the claims place no particular limits on the components of the media; the media is described wholly in functional terms. The claims are currently so indefinite that they cannot be meaningfully examined. The claims should particularly point out the physical and structural characteristics of the media that is used in the method. Because claims 17-27 depend from indefinite claim 16 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claims 19 and 20 refer to the "maximum **expected** cell count," which is confusing. It is not clear who or what is expecting the cells to be present in a particular

number. Furthermore, this term places no particular limit on the number. It is simply not clear what variable applicant means to reference. Clarification is required.

Claims 19 and 20 also refer to an amount of glucose to be consumed by the cells, but this amount is defined entirely in functional terms. It is not clear what amount is required or how the amount would even be measured. Clarification is required.

Claim 21 includes preferred embodiments, e.g. "CHO such as CHO-K1," which is improper. It is not clear whether the terms after "such as" are necessarily part of the claim or not. Clarification is required.

Claim 23 recites the abbreviations "EPO" and "PA" without defining the same in the claim. Clarification is required.

Claim 24 refers to "before glucose limitation occurs," which is confusing. It is not clear how this claim relates to the independent claim temporally. Clarification is required.

Claim 25 refers to "other nutrient media," but the independent claim refers only to one media. It is not clear how claim 25 relates to claim 16 spatially or temporally. Clarification is required.

No claims are allowed.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art

may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651